

### **REMARKS**

Claims 36, 40, 55, 56, 62 and 63 have been amended to recite sequence identifiers, support for which can be found in the Specification and Sequence Listing.

New claims 82-86 have been added. Support for these claims may be found in the paragraph bridging pages 8-9 of the Specification and in the original claims.

The claims have been amended to more clearly describe the present invention, and no new matter has been added.

#### **1. The Restriction Requirement**

The Examiner contends that the application contains 14 inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. The Examiner has defined the inventions as follows:

**Group 1**, claim(s) 1, 34-44, 46, 48, 50 and 52, drawn to a method of making an antibody with a modified heavy chain alpha 3 or mu domain comprising modifying the C-terminus 18 amino acid residues in order to reduce or eliminate the vacuolar targeting of the antibody.

**Group 2**, claim(s) 45, 47, 49, 51 and 53, drawn to a method of adding a J-chain binding capability to the heavy chain of an antibody by introducing a synthetic tail comprising amino acid sequence  $-(Xaa_1)_m C(Xaa_2)_n$ .

**Group 3**, claim(s) 54, 56, 58, 60, 62, 64 and 66, drawn to an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or more targeting signals.

**Group 4**, claim(s) 55, 57, 59, 61, 63, 65 and 67, drawn to an antibody comprising  $-(Xaa_1)_m C(Xaa_2)_n$  and capable of binding to a J-chain.

**Group 5**, claim(s) 68, drawn to a method of treating a disease comprising

administering an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or more targeting signals.

**Group 6**, claim(s) 69, drawn to a method of treating a disease comprising administering an antibody comprising  $-(Xaa_1)_m C(Xaa_2)_n$  and capable of binding to a J chain.

**Group 7**, claim(s) 70, drawn to a method of prophylaxis comprising administering an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or more targeting signals.

**Group 8**, claim(s) 71, drawn to a method of prophylaxis comprising administering an antibody comprising  $-(Xaa_1)_m C(Xaa_2)_n$  and capable of binding to a J-chain.

**Group 9**, claim(s) 72, 74 and 76, drawn to vectors and host cells comprising nucleotides encoding an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or more targeting signals.

**Group 10**, claim(s) 73, 75 and 77, drawn to vectors and host cells comprising nucleotides encoding an antibody comprising  $-(Xaa_1)_m C(Xaa_2)_n$  and capable of binding to a J-chain.

**Group 11**, claim(s) 78, drawn to a transgenic plant comprising a nucleotide encoding an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or more targeting signals.

**Group 12**, claim(s) 79, drawn to a transgenic plant comprising a nucleotide encoding an antibody comprising  $-(Xaa_1)_m C(Xaa_2)_n$  and capable of binding to a J-chain.

**Group 13**, claim(s) 80, drawn to an immunoassay comprising an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or more targeting signals.

**Group 14**, claim(s) 81, drawn to an immunoassay comprising an antibody comprising  $-(Xaa_1)_m C(Xaa_2)_n$  and capable of binding to a J-chain.

The Examiner alleges that the inventions listed in Groups 1-14 do not relate to a single general inventive concept under rule PCT Rule 13.1 because they lack the same or corresponding special technical feature. According to the Examiner, the corresponding technical feature of the invention is:

...an antibody molecule containing a heavy chain comprising a modification in the  $\alpha 3$  or mu domain, where the modification occurs within the C-terminus 18 amino acids in order to remove or reduce the effectiveness of vacuolar targeting signal sequences (Restriction Requirement, page 2).

The Examiner then contends that the combination of Frigerio et al. (2000), Vitale and Raikhel (1999), and Koide et al. (1999) reads on the technical feature of the invention, and concludes that the technical feature is therefore not special. The Examiner's reasoning for coming to this conclusion can be found on page 3 of the Restriction Requirement, and is not reproduced here. Applicants respectfully traverse.

Applicants submit that Frigerio et al. does not disclose the presently claimed invention. In particular, Frigerio et al. teaches that SIgA/G is partially targeted to the vacuole (whereas IgG is not). SIgA/G is a recombinant immunoglobulin comprised of heavy chains in which the variable domains and the constant  $C\gamma 1$  and  $C\gamma 2$  domains of the IgG  $\gamma$ -chain are linked to the constant  $Ca 2$  and  $Ca 3$  domains of the IgA  $\alpha$ -chain (Frigerio et al. page 1484, first paragraph of the Results section). Frigerio et al. speculates that a number of mechanisms/pathways such as ER stress, structural defects, certain cystein residues of the SIgA/G unit and/or the  $Ca 2$  domain could be involved in targeting SIgA/G to the vacuoles.

Applicants point out that the  $Ca 2$  domain is not equivalent to the presently claimed  $Ca 3$  and  $\mu$  domains. In addition, the  $Ca 3$  domain taught by Frigerio et al. is 130 amino acids, and Frigerio et

al. in no way contemplates antibodies with modifications to the C-terminal 18 amino acids of the C $\alpha$ 3 domain, as presently claimed. Frigerio et al. therefore fails to teach or suggest the Applicants' claimed invention.

The Vitale and Raikhel and the Koide et al. publications fail to rescue the deficiencies of Frigerio et al. These references disclose vacuolar sorting signals in plant proteins, and in no way teach or suggest antibodies having modifications to their C-terminal 18 amino acids of C $\alpha$ 3 or  $\mu$  domains. It follows that, even when combined, the prior art of record fails to teach all of the elements of Applicants' claimed invention.

Applicants further submit that the Vitale and Raikhel and the Koide et al. publications may not properly be used in an obviousness rejection. In particular, these references teach plant proteins and vacuolar sorting signals; whereas the present invention relates to antibodies. It is well known that antibodies originate from animals, and are not plant proteins. A person of skill in the art would have not expected an animal protein to include a sequence that functions as a plant vacuolar targeting sequence. The Vitale and Raikhel and the Koide et al. publications therefore teach away from and occupy a different field than the presently claimed invention; so they cannot be used in an obviousness rejection.

In view of the foregoing points, Applicants submit that Applicants claimed invention is novel and non-obvious over the prior art. Accordingly, the corresponding technical feature of the invention is indeed special under PCT Rule 13.1, and unity of invention in fact exists. Restriction is therefore improper.

Applicants also call the Examiner's attention to the fact that Article 27(1) of the Patent Cooperation Treaty does not permit any national law or national office to require compliance with different regulations relating to the contents of the international application. Thus, the U.S. application must be examined for unity of invention consistent with the Patent Cooperation Treaty, not just by giving verbal ascent to the unity of invention standard, but an actual application of the standard. See *Caterpillar Tractor Co. v. Commissioner of Patents and*

*Trademarks*, 231 USPQ 590 (Ed. Va. 1986). Since the restriction requirements imposed in sections 7-9 (Office Action, pages 6-11) are based on U.S. law, and not PCT Rule 13, Applicants respectfully submit that they are not applicable to the present application. Applicants therefore request that the Restriction Requirement be withdrawn in its entirety, and that all of the claims be examined in this Application.

In order to be fully responsive, **Applicants elect, with traverse, to prosecute the claims of Group 1** (claims 1, 34-44, 46, 48, 50 and 52). Applicants further submit that new claims 82-86, which depend from claim 1, should be included in Group 1.

## **2. The Election of Species requirement**

The Examiner has also imposed an election of species requirement. Applicants therefore elect to initiate examination with the following:

Xaa<sub>1</sub> = alanine

Xaa<sub>2</sub> = glycine

m = 5

n = 1

Applicants reserve their right to the examination of further species upon the Examiner's finding allowable subject matter with the initially elected species.

Claims 36-37, 45, 47, 49, 51, 53, 55, 57, 59, 61-63, 65, 67, 69, 71, 73, 75, 77, 79 and 81-86 are readable to the elected species, of which claims 36-37 and 82-86 are included in Group 1.


Favorable action and early allowance of all of the claims, which define patentable subject matter, are solicited.

Pursuant to the provisions of 37 C.F.R. 1.17 and 1.136(a), Applicants have petitioned for a one (1) month extension of the period to file a Reply to the Office Action issued August 23, 2006, to January 23, 2006. The required fee has been paid in connection with the filing of this response.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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